LETTERS TO THE EDITOR

Carbamazepine in the treatment of generalised tonic clonic seizures in juvenile myoclonic epilepsy

Juvenile myoclonic epilepsy is characterised by bilateral myoclonic jerks on wakening, and generalised tonic clonic seizures with onset in the mid-teens, which may be preceded by typical absences in 33% of patients.[1] Findings on EEG include bilateral spikes or multiple spike-slow wave discharges at 4-6 Hz with a normal background; about 30% of these patients show photosensitivity or focal abnormalities, or both.[1]

A particularly good long-term prognosis exists if compliance with valproate, the drug of choice for the treatment of juvenile myoclonic epilepsy, continues.[1-4] In the 8–20% of patients in whom full control cannot be achieved with valproate treatment alone, low doses of the second-line anticonvulsant drugs clonazepam, clobazam, or phenobarbitone may be needed.[1-3] Carbamazepine is not indicated for juvenile myoclonic epilepsy, with some reports suggesting that it may actually exacerbate seizures.[3 4] In view of this consensus it was of particular interest to us that in two patients with juvenile myoclonic epilepsy, generalised tonic clonic seizures but not absences or myoclonic jerks were controlled only after carbamazepine was added to valproate treatment.

CASE 1

This woman, aged 32 years, whose mother also has generalised tonic clonic seizures, has late onset congenital adrenal hyperplasia and juvenile myoclonic epilepsy with photosensitivity. Her first generalised tonic clonic seizure at the age of 14 years was induced by television; all others occurred on wakening. Generalised tonic clonic seizures were well controlled by carbamazepine (400 mg/day, plasma concentration 34 μmol/l), only six having occurred in 13 years, but violent myoclonic jerks on wakening and frequent, inconspicuous typical absences were resistant. Neurological examination was normal and EEG findings were consistent with juvenile myoclonic epilepsy and photosensitivity, but showed some inconsistent focal abnormalities. During her first pregnancy at the age of 29 years, the myoclonic jerks disappeared. Within a few days of the birth of a healthy son, they returned every morning after wakening, and were violent enough to make her drop her baby. Six months later she had her first generalised tonic clonic seizure in three years. Juvenile myoclonic epilepsy was diagnosed and valproate (1 g/day) added. This fully controlled the myoclonic jerks and absences, and carbamazepine was withdrawn completely over two months. Three weeks later she had a second generalised tonic clonic seizure, associated with sleep deprivation and stress. Valproate was increased to 1·5 g/day but after two weeks a further three generalised tonic clonic seizures occurred at weekly intervals, prompting an increase in dose to 1·7 g/day. These seizures immediately preceded her second pregnancy. In spite of taking valproate at 2·0–2·2 g/day (plasma levels were consistently higher than 700 μmol/l) a further three generalised tonic clonic seizures occurred at 21, 22, and 27 weeks' gestation, again when sleep-deprived. Carbamazepine (400 mg/day increasing to 600 mg/day) was then added. The remainder of the pregnancy was uneventful and no generalised tonic clonic seizures, myoclonic jerks, or absences have occurred for 29 months, despite decreasing the valproate dose to 1000 mg/day.

CASE 2

This 20 year old woman, had a febrile convulsion at the age of 3·5 years. Typical absences, myoclonic jerks, and generalised tonic clonic seizures occurred in her mid-teens with no particular circadian distribution. The seizures were spontaneous or precipitated by television, video games, anger and emotion, and sleep deprivation. Neurological examination and MRI were normal. Results of EEG support a diagnosis of juvenile myoclonic epilepsy with photosensitivity, but marked alternating focal abnormalities were also found in follow-up EEGs.

Valproate (1 g/day) controlled the generalised tonic clonic seizures initially but had little effect on the myoclonic jerks, and produced a large weight gain. Phenytoin made her hirsute and at a saliva concentration of 5·4 μmol/l was of no benefit. At her first visit to us she was taking valproate (1200 mg/day; plasma levels >306 μmol/l), clonazepam (1 mg/day), and phenytoin (250 mg/day), and as a result of pre-examination stresses her myoclonus was worsening. A previous two week trial of carbamazepine (400 mg/day) alone had been unhelpful. Phenytoin was withdrawn slowly. With the combination of valproate (1500 mg/day) and clonazepam (1.5 mg/day) absences were minimised, myoclonic jerks were nocturnal only, but the generalised tonic clonic seizures persisted. Carbamazepine (1200 mg/day) was added to this regimen without side effects and no further generalised tonic clonic seizure has occurred in 15 months.

These cases of definite juvenile myoclonic epilepsy and photosensitivity show that carbamazepine combined with valproate was more effective than valproate either alone or with clonazepam in preventing generalised tonic clonic seizures. Carbamazepine alone did not prevent generalised tonic clonic seizures, myoclonic jerks, or absences in either patient and although valproate was efficacious against the latter seizure types, the combination of the two drugs was necessary for full generalised tonic clonic seizure control. Interestingly, the two patients had some focal abnormalities on EEG in addition to findings typical of juvenile myoclonic epilepsy. Valproate is the acknowledged drug of choice for this syndrome, producing a rapid and sustained reduction or abolition of generalised tonic clonic seizures, myoclonic jerks and absences in more than 80% of patients.[1-4] In those rare instances in which generalised tonic clonic seizures prove recalcitrant to treatment, however, and particularly if there is some evidence of focal discharges at EEG, the combination of valproate with carbamazepine may successfully abolish them. These patients exemplify the need for syndrome-related drug trials and for a consideration of possible pharmacodynamic interactions between various drugs used to treat epilepsy.

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Intracranial chordoma with a novel symptom

The case is described of a novel presentation of an adult with an intracranial chordoma. The onset was relatively acute with neck pain and lower cranial nerve involvement producing an unusual symptom related to head movement and posture. The tumour has followed an aggressive course in spite of radical surgery and radiotherapy.

A 40-year-old man presented with cervical and occipital pain which had persisted for four months. No neurological deficit was found and a diagnosis of cervical spondylosis was made. Plain radiographs of the craniovertebral junction and neck were normal.

Two months later he presented again, reporting that on flexing his neck or lying horizontal he could not move his tongue properly and was unable to speak. These symptoms resolved within 30 seconds of sitting up or raising his head. He was referred to the neurology department where wasting of his tongue, more marked on the right, with deviation of the median raphe to the right was noted. An inability to speak and to move his tongue on flexing the neck was shown but lingual sensation to touch and pin-prick was normal. The remainder of the neurological examination was normal and ear, nose, and throat assessment confirmed normal palatal movement and sensation.

After a few weeks his neck pain and the positional symptoms affecting his tongue resolved and were replaced by persistent dysarthria with difficulty in propelling saliva, food or fluid to the back of the mouth. There was no choking or nasal regurgitation. During this period he developed wasting of the extensor neck muscles, especially on the left side, and of the sternomastoids.

Enhanced CT and MRI showed a destructive mass lesion, thought to be a chordoma, extending from the clivus to the anterior margin of the foramen magnum. A transoral resection of the tumour was performed and complete clearance was felt to have been achieved. Histology showed the characteristic appearance of a chordoma: nests and chords of polyhedral tumour cells, often with vacuolated "bubbly" cytoplasm (physaliphorous cells) and uniform round nuclei, were surrounded by a plentiful mucinous matrix.

The patient made a good recovery after the operation, with some improvement of speech and swallowing. There was residual wasting and weakness of the tongue. Six months after the operation the bulk and power of the sternomastoids and neck extensor muscles had almost returned to normal.

Seven months after the operation the patient developed diplopia, his swallowing started to deteriorate again, and his voice became hoarse. At this time he was noted to have a partial left sixth nerve palsy and a left Horner's syndrome.